COLLEGE OF ENGINEERING
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DEPARTMENT OF BIOMEDICAL ENGINEERING

An Open Source Imaging Platform for Small Animal Imaging and Therapy

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Abstract

An open source medical device has the benefits of a cheaper cost and more collaboration amongst researchers. A combined computer tomography (CT), positron emission tomography (PET) and radiation therapy (RT) system is being developed in the spirit of open source technology. The combination of these systems has the added benefit of correlating data among the imaging systems and using this data for precise radiation therapy treatment. The CT system uses X-ray radiation and detectors to produce 2-D and 3-D cross-sectional images of anatomical structures at high resolution. The PET system uses radioactive tracers to highlight metabolic activity of different biological structures. The RT system uses high intensity X-ray radiation to non-invasively obliterate cancerous cells in the body. A table of specifications for various components of the different systems has been developed with the intention of designing a combined system with the minimal number of components.

Open Source

In collaboration with the Morgridge Institute for Research, the client is developing an Open Source Medical Device (OSMD) program, which would provide researchers around the world free access to a device's design and development. The OSMD program brings researchers together, encouraging cooperation during the design process. Another advantage to open sourcing is that it makes expensive instruments and technology available to research groups with limited funding. As all software and hardware specifications are accessible, researchers can build and design the system for their own use, avoiding buying an expensive unit directly from one manufacturer [11].

Computed Tomography Background

Computed Tomography (CT) is a common technique used to obtain 2-D or 3-D images that display internal structure. CT by itself is not a specific imaging system; instead the term is used to describe the method in which an image is reconstructed. Positron Emission Tomography (PET), Single Photon Emission Tomography (SPECT), and x-ray imaging all use CT to create 2-D or 3-D representations from projections. For the purposes of this project, x-ray CT will be the primary technique implemented in the imaging device. In x-ray CT systems, electromagnetic radiation is applied to an object and attenuated as seen in Figure 1. Detectors located opposite the x-ray source measure the remaining radiation, creating a projection of how the objected scattered the energy. The x-ray source is then rotated about the object to create an array of projection data, which can be used to reconstruct a 2-D image. By moving the object in the y-direction as seen in Figure 1, multiple slices can be obtained and used to create a 3-D image.
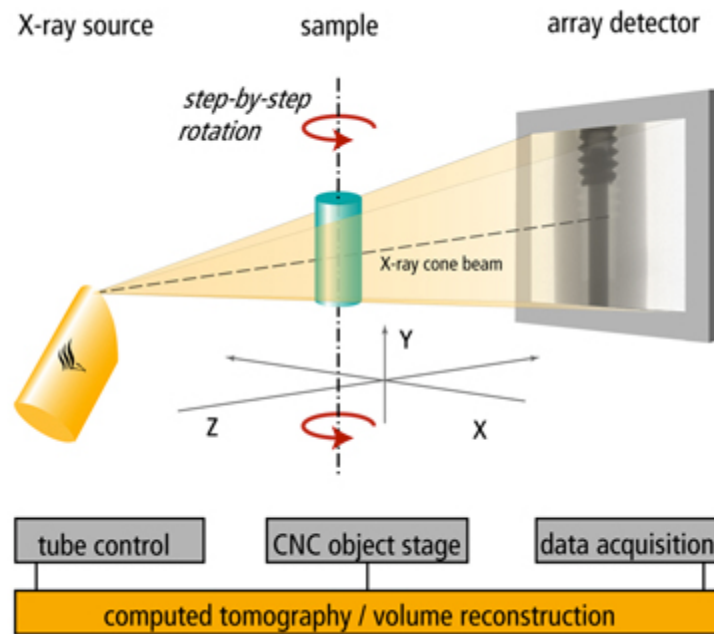
Figure 1. Method of X-Ray CT data collection. [8]

In order to create x-rays, one must first understand the nature of electromagnetic (EM) radiation. X-rays are a subclass of electromagnetic radiation occurring with energies between 20keV to 120keV [6]. Electromagnetic radiation is primarily the result of both an oscillation electric and magnetic field. However, while it can be modeled as a wave, such radiation also has particle properties, the particle being known as a photon. This type of radiation is known as non-ionized radiation since it does not contain a charge. Thus, the energy of EM radiation comes from kinetic energy of photon's motion. The relationship between the energy of the photon and the frequency of its oscillations as a wave is given by:
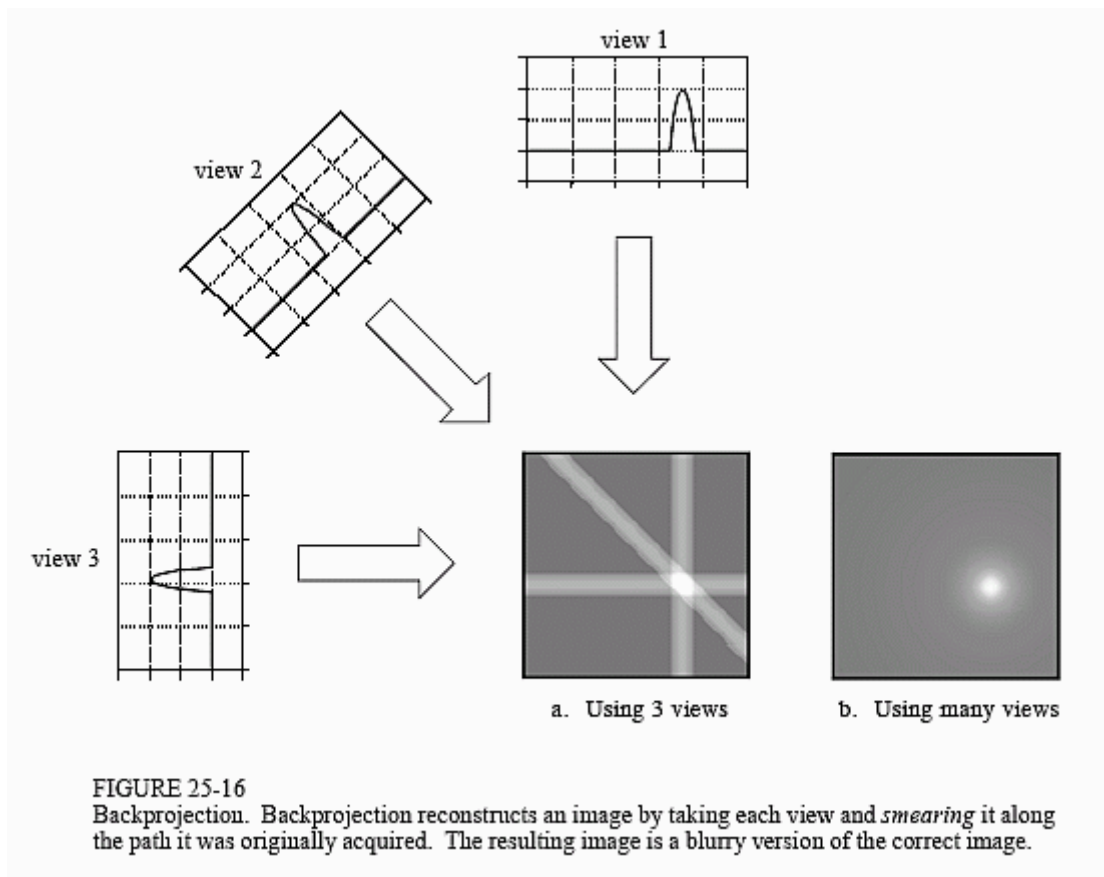
$$E = hf$$

Where E is the energy, h is Plank's constant, and f is frequency. Thus, in order to create x-rays, one must create an event in which energy is released from the system. A common method is to collide electrons with a target and by conservation of energy. As the electrons slow down, they release energy by conservation, also called Bremsstrahlung radiation [6]. Thus by adjusting the speed in which the electrons hit a target, we can adjust the energy of radiation produced.

Since x-rays can be thought of as a particle, it is clear to understand their interaction with other matter. If an x-ray hits an electron, it can transfer its energy to set that particle in motion, known as the photoelectric effect. Alternatively, an x-ray can come in close contact with an electron or proton and scattered because of the electric field. It is also possible for both events to occur, known as the Compton Effect [6]. Here, an x-ray transfers part of its energy to an electron and then scattered with a reduced energy. These three types of interaction between radiation and matter are exploited with

CT imaging. Since these interactions will be dependent on the electron density of an object, the data collected from x-ray CT represents the contrasts between areas of high density from areas of low density.

Data of how x-rays were attenuated by an object can be collected using photodiodes or photomultiplier tubes. Both methods utilize the photoelectric effect, which converts the x-ray energy to a measurable voltage change. Through the use of an array of these devices, we can discretely measure x-rays after they have passed through an object. After a certain exposure time, the voltage measure by each photodiode represents the sum of x-ray energy in that given period. However, since the object is assumed to be a continuous structure with a continuous distribution of x-rays passing through it, care must be taken when sampling the output. Specifically, the Nyquist criterion states that we must sample the data at twice the spatial frequency to avoid aliasing when reconstructing the image. Once the data is collected, a distribution of the x-rays hitting the detectors can be displayed for that projection.

FIGURE 25-16
Backprojection. Backprojection reconstructs an image by taking each view and *smearing* it along the path it was originally acquired. The resulting image is a blurry version of the correct image.

Figure 2. Method of filtered back-projection for reconstructing an image from the response function at different angles. [13]

As seen in Figure 2, projection data of the object is then taken by rotating the gantry at different angles. As seen in diagram, increasing the number of angles used to collect

increases the quality of the image. However, in order to display the original object from the project data, a reconstruction algorithm can be used. One of the most common methods of reconstruction is through filtered back-projection. In this method, a 1-D Fourier transform is taken from the projection data at a given angle. This can then be represented as a 2-D object in spatial frequency space or k-space. A ramp filter is then applied to reduce replication of spatial frequencies in the center of the image. Using the projection angle, the 2-D data is then transformed into the proper coordinates and a 2-D inverse Fourier transform is performed, resulting in the image of the object [6]. An example of an x-ray CT image generated through this method can be seen below in Figure 3.


Figure 3. Example of a CT image reconstructed depicting the abdomen of a human patient. [12]

A number of factors affect the quality and resolution of the image. As already discussed, the sampling rate must be in accordance to the Nyquist frequency. If the object is under sampled, the final image will be blurred. Thus it is important to correctly determine the spacing between the photodiodes in the detector. Also, the size of each detector will limit the resolution. Ideally the width of each detector should be zero to obtain maximum resolution, but since this is impossible the image cannot have a spatial density larger than the width of each photodiode. Another factor that affects resolution is the detection scattered x-rays. To reduce this occurrence, a collimator can be added to filter any x-rays not traveling in a straight line. Finally, the x-ray energy used when imaging will affect the quality of an image because high energy x-rays will not be

attenuated as effectively as low energy x-rays since they have much larger forward momentum.

CT Specifications

In order to design an x-ray CT system, a number of specification regarding the x-ray source, detector type, gantry dimensions, collimators, filters, data collection, and reconstruction software. In Figure 4 below, a basic overview of the components in an x-ray CT system can be viewed.
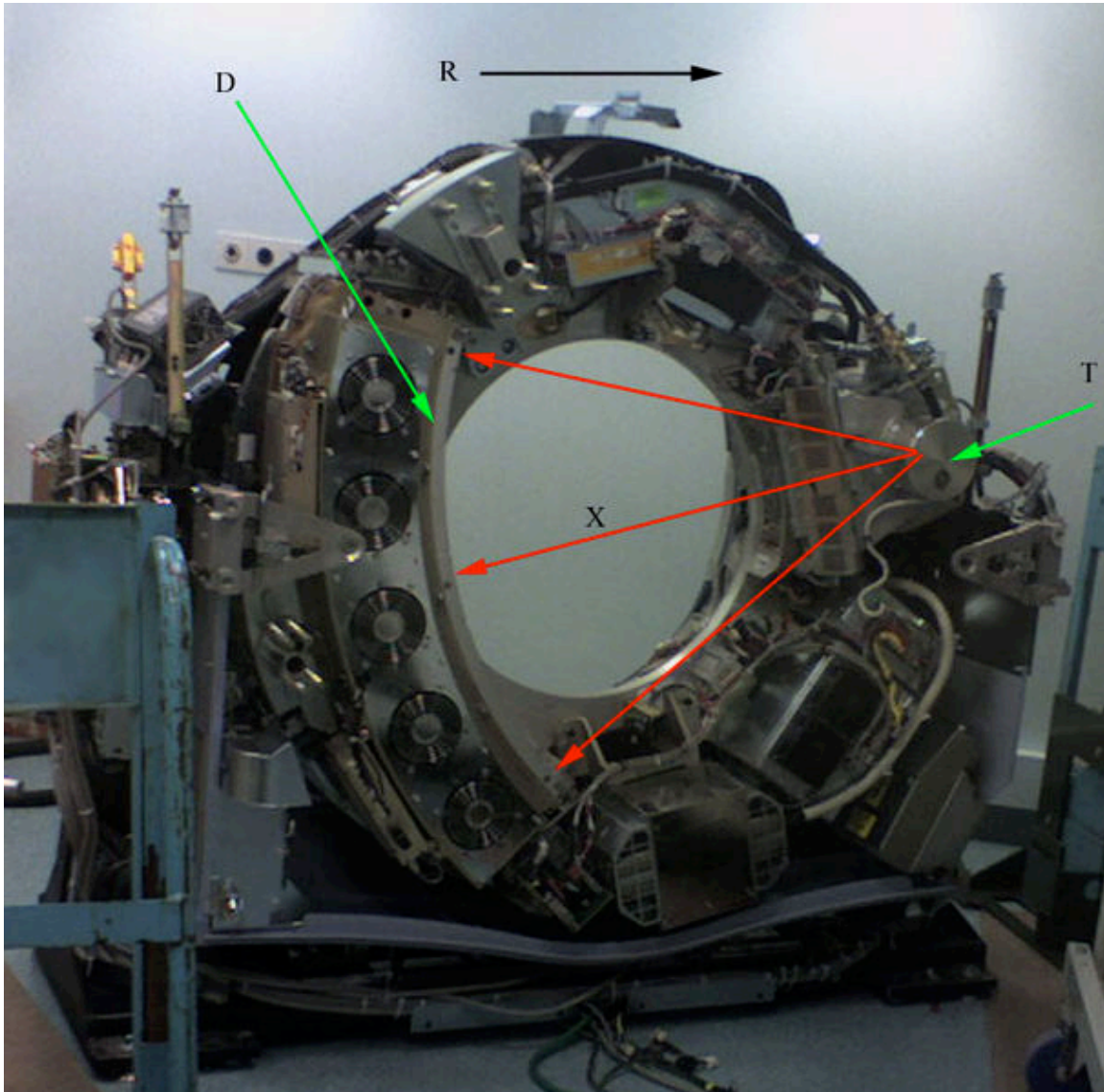
Figure 4. Image displaying the internal components of an x-ray CT machine. T represents the x-ray tube. X are the x-rays produce that travel through the patient. D is the detector array. R is the direction of gantry rotation. Ref: [http://en.wikipedia.org/wiki/File:Ct-internals.jpg].

In Table 1 below, a list of specifications for the CT system are described. Since CT imaging is only one component of the system being designed, specifications

regarding the gantry and cooling system will be discussed elsewhere. It was decided that the x-ray source should output energy between 50-100kVp. This would be enough energy to fully penetrate the object while providing adequate contrast and attenuation. Also, the focal spot of the x-ray source would need to be less than 10 microns to achieve good image resolution. A 0.5 mm copper sheet and a 1mm aluminum sheet were chosen as filters because of their ability to absorb soft x-ray energy. The geometry for data acquisition will be fan beam because of its simplicity and lower cost of production. However, collimators using fan beam geometry require an addition processing to account for changes in the focal position. Silicon photodiodes were chosen as detector elements because of their lower cost, size, and efficiency. Overall, the system designed should have a resolution between 20 to 40 microns.

Table 1. Specification for the CT imaging system.

X-ray Source Energy	50-100kVp
Focal Spot	<10 micron
Filters	0.5mm Cu and 1mm Al
Acquisition Geometry	Fan Beam
Detector	Silicon Photodiodes
Detector Resolution	20-40 micron

Positron Emission Tomography

Positron Emission Tomography (PET) is a nuclear imaging modality that is used to show physiology. The basic principle involves using a radionuclide that decays by positron emission. Positrons are the antiparticle for electrons, and when the particles collide, they annihilate. This produces two gamma rays that travel in opposite directions at 511 keV [6], which is the mass of an electron. For imaging, the radionuclide is attached to a metabolite that is injected into the body. The positron emission and subsequent annihilation can be used to image metabolic activity and physiology. The basics of PET from a systems perspective can be broken down into three major parts— the radionuclide, the detector array, and the imaging reconstruction method.
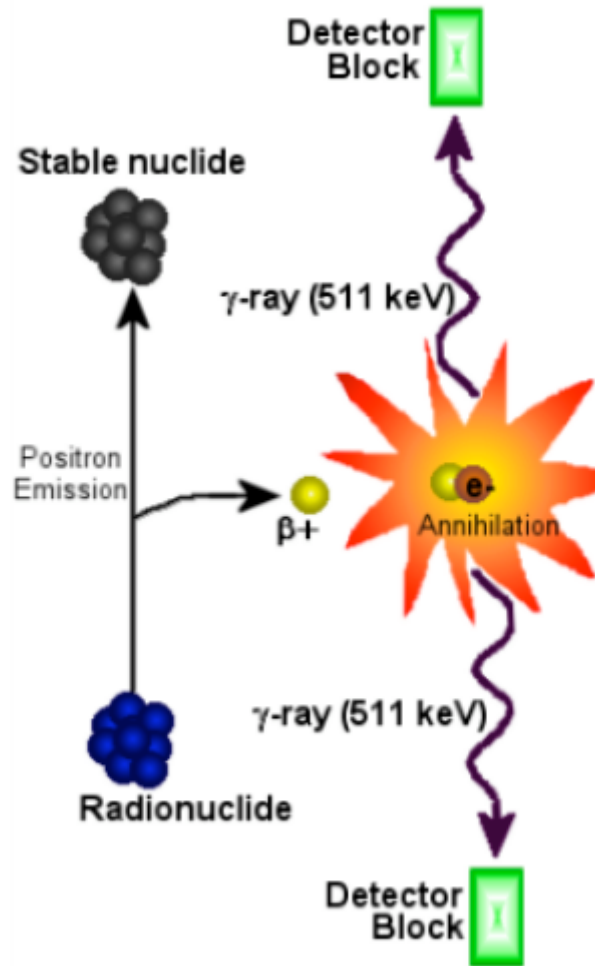
Figure 5. Diagram showing the basics of PET data collection.

The radionuclide that is used for PET varies based upon the system or organ of interest. Commonly used nuclides include C-11, N-13, F-18, Cu-64, I-124 [6], and they can be conjugated with biologically active molecules to determine metabolism. For example, the most commonly used radionuclide, flurodeoxyglucose (FDG) uses F-18 and acts as a glucose analogue [5]. This can be used to image the brain, the heart, and lungs for metabolic activity, or used in oncology to image tumors. The only downside to this method of imaging is that most radionuclides used have short half-lives, usually less than two hours. This requires that it either be made onsite or shipped quickly to clinics that have PET scanners, both of which are very costly.

As mentioned previously, the radionuclides used decay by positron emission—the positrons collide with electrons in the body and produce two gamma rays traveling in opposing directions at 511 keV. These gamma rays are used to indicate an annihilation event when they strike the detector blocks. The detector blocks make up the next major component of the PET imaging system. In the basic block, a scintillation crystal is connected to a photomultiplier tube (PMT). Modern detector blocks have modified this

principle, using a single crystal which has been cut to make a smaller array of crystals. These cuts have an opaque reflector which improves the resolution of detection by controlling the light distribution that reaches the PMTs.
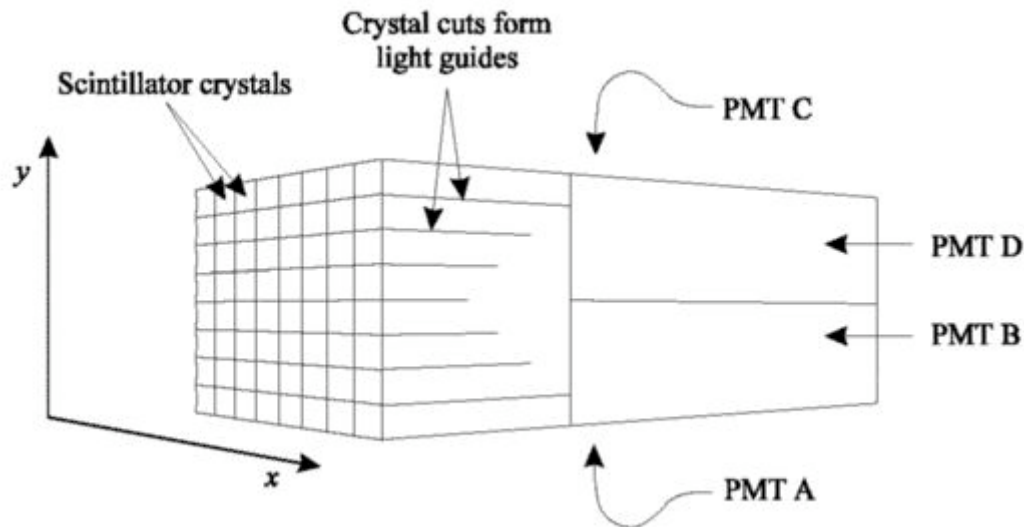

Figure 6. A diagram showing a PET detector block [18].

The choice of scintillator crystal is also important for determining the efficacy of imaging. The detection efficiency is determined by the linear attenuation coefficient of the material as well as the material thickness. The linear attenuation coefficient is given by how easily a beam of light can penetrate the material. As such, a high attenuation is desirable since it indicates that light can penetrate easily. Commonly used materials for detector crystals include BGO (Bismuth germanate), LSO (Lutetium oxyorthosilicate), and BaF_2 (Barium Fluoride) [6]. The PMT is a type of light-detecting vacuum tube and is analogous to an operational amplifier for electric currents. Incoming light is amplified to produce a larger current than would be produced by the incident light, and the resulting current carries the signal of a detection event to the logic system.

In order to produce an image, a few additional characteristics are needed. By noting the time difference between detection events, it is possible to determine the location of the original annihilation event. It is important to note that only events that occur on opposing blocks are recorded—there are scattering gamma rays and random noise that also strike the detector blocks, but these are discarded. A series of opposing detection events over an extended period of time produces enough data to render an image. Similar to CT, the filtered back-projection method is used to create the PET image.

PET Specifications

For our PET system, we need to establish a few basic parameters with which to frame the specifications. It is important to consider that the radionuclide used will be left entirely to the discretion of the clinician or researcher, and as such, all the other equipment must work correctly. The important items to consider are the detector blocks and their components—the scintillation crystals used, the arrangement of the crystals, the

PMTs used, the combination of crystals and PMTs, and how the blocks form a detector array.

For a scintillator crystal, we opted for LSO. LSO has a good linear attenuation coefficient, is fairly inexpensive, and it also came at the recommendation of our client. The crystals will be arranged in a 20 x 20 array with 64 blocks, and each crystal will be 10 mm thick. The size is ideal for a small animal system, and a 20 x 20 array will provide a reasonably good resolution. The 64 block size came suggested from the client as well. The PMT used has yet to be finalized, but we have considered a model from Hamamatsu [17]. Still to be determined is the method of placing PMTs and crystals and the method of arranging the blocks to form the detector ring.

A more detailed list of specifications can be found in Appendix A: Product Design Specifications.

Radiation Therapy

Radiation therapy works by sending ionizing radiation into the body to kill unwanted cells. Commonly, a CT scan is taken of the area to determine the exact size, shape and most importantly location of the tumor. This data can then be fed into a computer and a treatment planning system can be used to develop the most effective treatment. Frequently, intensity modulated ration therapy treatments (IMRT) are used. This involves changing the intensity of the radiation and the collimator size for each beam of radiation [2]. A picture of this type of planning is shown below. High intensity X-rays are then shot into the body. Shape and intensity of the beam are modulated, using components described below, to ensure that only unwanted cells are obliterated. When the x-rays interact with the cells, it changes the genetic make up of the cells, causing them to die instead of proliferate. There are two different types of radiation that cause cellular death: direct and indirect. The direct method enters the cell and directly cuts the DNA and proteins in half. The indirect method enters the cell and ionizes the water molecules. This causes the formation of free radicals, which degrades the cell [3]. This procedure is also effective because cancerous cells divide much faster than healthy cells, so the cancerous cells would die almost immediately. The healthy cells, on the other hand, have time to recover from the radiation and will not be affected so harshly. Overall, radiation therapy has proven to be an effective non-invasive alternative for cancer treatment in humans.

Figure 7 - Image of a IMRT plan showing the exact location and size of the radiation beams [10].

There are three major hardware components involved with the delivery of the radiation: Linear accelerator, collimator and a dosimeter. First, there needs to be some source of radiation to put into the body and this comes from a linear accelerator. A linear accelerator accelerates an electron beam to a very high speed. This beam then strikes a target and X-ray photons are emitted. For radiation therapy purposes, the X-ray photons that are emitted must be of very high intensity and thus are frequently called orthovoltage X-rays.   The intensity of the X-ray beam emitted can be modulated through the final speed of the electron beam coming out of the linear accelerator. This is one of the many ways that the treatment can be specialized to each patient. The x-rays are then passed through a collimator, which determines the size of the beam emitted into the body. A collimator is made of metal leaves, frequently lead, that can be moved relative to each other to produce a shape similar to the shape of the tumor. All other X-rays are deflected by the metal leaves and absorbed in the machine. Finally, it is very important to know exactly how much radiation is coming through the collimator at each time, which is where the dosimeter is needed. Most frequently, ion chambers are used as dosimeters in radiation therapy. This system is composed of a small chamber filled with electrically charged gas particles (ions). When X-rays enter the system, the ions dissociate and cause an electric current between the two plates, which are acting as electrodes [3]. This information can be interpreted by a computer to give the exact amount of radiation coming out of the collimator. It is important that the patient not be over radiated, but also that there is enough radiation going into the body to be effective.

RT Specifications

While there are many specifications relating to the hardware components of the radiation therapy system, there are a few in particular that will be discussed here. The orthovoltage tube (X-ray generator) should reach 250 kVp (peak kilovoltage), which is sufficient to kill any cancerous cells in the body. It should also have two focal spots to increase the maximum amount of power that can be used. A higher power requires a

larger focal spot, this is not always needed, and therefore having two separate focal spots provides the researcher with a choice between the two. The larger of the two focal spots should be 2 mm in diameter while the smaller should be around 0.4 mm. Also dealing with the orthovoltage tube is the problem of maintaining the correct temperature for the linear accelerator. It must be maintained within 2°C and this will be accomplished with a water-cooling system. There are a few different systems commonly used for dosimetry, including quartz fiber, silicone film, thermoluminescence and ion chambers but for this project an ion chamber will be used. Ion chambers give highly reproducible, accurate results and are very accessible. A suitable dosimeter will be selected for use with this project. Finally, the last hardware component that is involved with RT systems is the collimation system. The collimator should be comprised of a type of metal, particularly W, Cu, brass or Pb. The collimator should have a thickness of 2 mm and should be comprised of at least 120 leaves. Programming and movement will be discussed once the software side of the project is worked on. These are the basic specifications for the radiation therapy system in this project.

Combination Systems

The first device in development for this project is an open source small animal research platform that integrates positron emission therapy (PET), computed tomography (CT), and radiation therapy (RT). A system for small animals was chosen because it would face fewer regulatory obstacles when compared to a human system. Also, small animal research serves as important and useful prototype modeling for human medicine [11].

Several RT/CT and CT/PET combination systems currently exist for both human and small animals, although technology in the small animal system area is less advanced. Combination systems are important because images captured from individual systems can be superimposed, allowing their respective information to be correlated [1]. As PET provides relatively low-resolution images of selected metabolic activity and CT provides high resolution images of anatomical structure, a CT/PET system allows researchers to pin-point the location of metabolic activity by fusing the two images. These techniques are used to detect cancers, determine the efficacy of treatment, and map normal organ function [1]. In a similar manner, CT/RT systems are used to find the exact shape and location of treatment areas, such as tumors, in order to coordinate the most appropriate and effective radiation treatment plan.
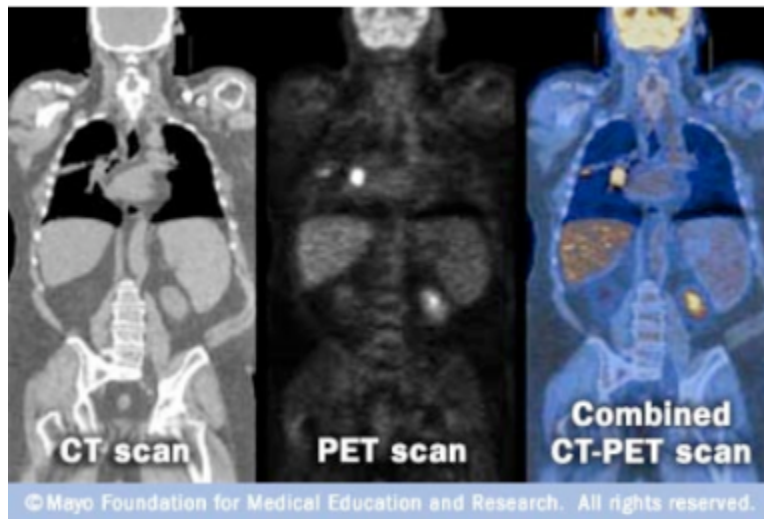
Figure 8 - A comparison of images gathered from CT and PET and the superimposed image showing the increased metabolic activity at anatomical locations.

Combination System Specifications

Although this project involves three separate systems, there are many components that are the same among all of them. These components include the couch, bore, motor, and beam shielding system. The couch system should have linear movement of 0.125 mm in all three planes and should be able to rotate 0.05° for precise positioning of the patient. The bore should have an interior diameter of 12 cm. The majority of the system should be made of plastics, but lead shielding will be needed to block any harmful stray radiation. Although specifications have not been developed for it, the motor is another system that needs to be considered in the future. A motor is required not only for moving the couch in and out of the machine, but also for moving the radiation source around the bore. Finally, a data acquisition system also needs to be considered. There is a great deal of information coming from these systems and it is very important to store and interpret this data. These are some of the more important specifications for the combined systems. This list should grow significantly as the project continues to progress.

Conclusion and Future Work

In conclusion, open sources medical devices can be used to reduce costs, encourage cooperative research, and expand availability. The first project to be included in the open source medical device organization will be the design of a combination CT, PET, and RT system for small animal imaging. In order to complete this design, a full specification list along with vendors for each component must be created as well as a 3-D model of the system, which would need to meet FDA approval. Radiation simulation and dosimetery calculation must be performed to assess the dose to the animal and necessary shielding needed to protect people in the surrounding area. Once the final specification and design are complete, existing parts can be purchased and custom parts such as the gantry can be fabricated. The system will need to be rigorously tested and calibrated to

ensure the design appropriate for a hospital or research setting. By designing a small animal imaging system, a scaled up version for human use could also be developed in the future.

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Appendix A

Product Design Specification - V1.4

Date: March 10, 2009
Project Title: An open-source imaging platform for small animals
Team Members:

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Problem Statement:
The overall aim of this project is to develop an open source small animal imaging and therapy platform that integrates imaging (e.g., Computed Tomography (CT), Positron Emission Tomography (PET)) and therapy (e.g., radiotherapy (RT)) together. This system will be designed on a flexible platform, enabling researchers to build their own system according to the available resources and needs. The specific aim for the design project is to provide initial design of such an open source imaging/therapy platform and potentially start prototyping the system at the fast prototyping system at the Morgridge Institute for Research (MIR).

Client Requirements:
- Complete list of specifications necessary for the design of a small animal imaging system
- System should be able to perform PET, CT, and radiation therapy
- Each type of imaging or therapy modality should be independent (e.g., an example device could only incorporate CT or only CT/RT)
- The development should be open source (i.e., all intellectual property is publicly available)
- The final product should have software and hardware completely ready to go in a "plug and play" format

Physical and Operational Characteristics:
- The device is to be used on small animals (e.g., rats and mice)
- The system should be able to incorporate any combination of PET, CT, and RT.
- Couch positioning, data acquisition, and data storage should be independent of any imaging/therapy modality.
- Each imaging/therapy modality will have its own level of specification

Miscellaneous:
Initial specifications for the imaging/therapy modalities and the overall device systems can be found in the tables below.

Radiation Therapy:

Systems	Specifications	Vendors
Radiation Therapy System		
Orthovoltage tube	2 Focal spots, 250 kVp max	Seifert ISO VOLT 225 M2, Seifert X-ray, Lewistown , PA Nucletron Selectron HDR system (Ir core)
Large focal spot	0.4 mm	
Dose Monitoring system	detectors-ion chamber, Radiochromic films	Exradin Ion chambers - http://www.standardimaging.com
		Ion Chambers - IBA Dosimetry, Bartlett, TN
Primary collimation system	Material-W, Cu, Brass	
MLC leaves: W or Pb	thickness - 2 mm, # leaves?	Millenium MLC - 120 leaves - Field size = 40 cm x 40 cm - Varian Medical Systems
Beam control system		Standard Imaging, Middleton WI http://www.standardimaging.com/
Target cooling system		
Motor	Same used for CT	
Animal Positioning System - Table	0.125 mm, 0.05° rotational	Servo Systems Co. Montville, NJ
Physical Platfrom	Made with plastics	

CT :

CT system	Specifications	Vendor
Bore diameter	12 cm	
X-ray source	Tungsten anode, 50-100 kVp	
Focal Spot	< 10 micron,	0.3mm Seifert X-ray
Filters	0.5 mm Cu, 1 mm Al	
Flat panel Si (amorphous) detector	resolution: 20 - 40 micron, 0.25 mm^3 voxel resolution Fan beam, FOV= 10 cm X 10 cm	Perkin Elmer, Fremont, CA
Image reconstruction system	Feldkamp projection for CT	
Motor	same as for RT system	
Three dimentional Digitzer	MIcroScribe3DX, Immersion Corp, SanJose, CA	
Animal Positioning System - Table	0.125 mm, 0.05° rotational	Servo Systems Co. Montville, NJ

PET:

PET system	
LSO detector crystals	10 mm thick, 64 blocks 20 by 20 array
Timing resolution	312 ps
Transmission source	Co-57
Image reconstruction system	Filterback projection for PET
PMT	http://sales.hamamatsu.com/assets/pdf/parts_R/R1450.pdf

Other Systems:

Couch positioning system	
Data acquisition system	
Treatment planning system	Wisc plan
Data management System	
Beam shielding system	Ph shielding
Power control system	
Power backup system	
Fail Safety System	
Report verifying system	
QA system	
PACS system	
Data base management system	
Scheduling system	
Electronic recording system	